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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:	Examiner: J. Reeves
Chatterjee et al.	Group Art Unit: 1813
Serial No.: 08/372,676	
Filing Date: 01/07/95	
For: Anti-idiotype monoclonal antibody 1A7 and use for the treatment of melanoma and small cell carcinoma	

DECLARATION UNDER 37 CFR 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, SUNIL K. CHATTERJEE, Ph.D., do hereby declare as follows:

1. I have been a collaborating investigator with Malaya Chatterjee and Kenneth Foon, inventors for the above-referenced patent application.

2. I am a Member of the Markey Cancer Center in Lexington, and am an Associate Professor in the Department of Obstetrics and Gynecology, University of Kentucky. My research expertise includes the field of molecular biology and genetic engineering. A copy of my *curriculum vitae*, describing my background and qualifications, accompanies this Declaration as *Exhibit C*.

3. I have obtained the nucleic acid sequence and the corresponding amino acid sequence for the heavy and light chain variable regions of monoclonal antibody 1A7. This data, along with the method used to obtain it is provided in *Exhibit A* attached to this declaration.

4. The heavy and light chain amino acid sequences were compared using the BLAST algorithm at the National Center for Biotechnology Information with all sequences available from the PDB, SwissProt, PIR, SPUpdate, GenPept, and GPUpdate databases. The comparison was performed on December 16, 1995.

5. Amongst the 50 database sequences matched most closely to that of the 1A7 light chain variable region, none was identical. 1A7 differed from the five closest sequences by 2 substitutions at residues 50 and 55, which are contained in the second complementarity determining region (CDR2). The two differences at these positions were non-conservative substitutions, and persisted in comparisons with other light chain sequences.

Panel A of *Exhibit B* provides a comparison of the 1A7 light chain sequence with the 15 closest sequences found in the BLAST search. Residues identical to those in 1A7 are indicated with a period.

6. Amongst the 50 database sequences matched most closely to that of the 1A7 heavy chain variable region, none was identical. The following summarizes the main points deduced from the comparison.

- The closest match was with a heavy chain fragment beginning at residue 9 (designation gp|M36221|MUSIGHAEB_1). There were 6 substitutions between

residues 1 and 97 (before the VDJ junction), 6 substitutions after residue 97, and 1A7 was shorter about the VDJ junction by 2 residues.

- The closest match with a full length heavy chain variable region had the following features (designation gp|U01185|MMU01185): There were **10** substitutions between residues 1 and 97, **7** substitutions after residue 97, and 1A7 was shorter about the VDJ junction by **3** residues.
- 1A7 differed in length from all sequences but one, due to insertions or deletions of 1 to 8 residues about the VDJ junction. For the sequence of equal length (designation pir|S11106|S11106), there were **18** substitutions between residues 1 and 97, and 8 substitutions after residue 97.
- All other comparisons showed at least **14** differences between residues 1 and 97.
- All other comparisons showed at least **4** differences after residue 97.
- All other comparisons showed a total of at least **22** substitutions, insertions or deletions along the entire variable region.
- Differences appeared throughout the variable region.

Panel B of *Exhibit B* provides a comparison of the 1A7 heavy chain sequence with the 15 closest sequences found in the BLAST search.

7. Amino acid consensus sequences of the 15 most closely matched V_L and V_H regions were designed, and compared with the 1A7 sequences. This is shown in Panel C of *Exhibit B*. Identical residues are marked with a period, and CDRs are overscored with asterisks.

Other than splicing differences about the VDJ junction, there appear to be about **16** differences between 1A7 and the prototype sequences. Two of these differences are present in

the light chain; 14 are present in the heavy chain. Seven differences occur in the CDRs, while nine occur in the variable region framework.

8. The sequence data described herein were obtained no earlier than about July 24, 1995. The 1A7 sequence data have not been disclosed except under terms of confidentiality. The data were included in a recent grant application made to the National Institutes of Health under terms of confidentiality, and it is my understanding that the data will remain confidential until the grant is approved. It is my understanding that a decision on the application has not yet been rendered.

9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

3/8/96
Date

Sunil Chatterjee
Sunil Chatterjee, Ph.D.